Table
Descriptive Characteristics of Subchondral Tibia Cadaveric Specimens

Variable	Cadaver 1	Cadaver 2	Cadaver 3	Cadaver 4	Cadaver 5
Race	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian
Sex	Male	Male	Female	Male	Female
Age (years)	72	53	57	76	78
Height (m)	1.75	1.70	1.64	1.73	1.68
Weight (kg)	59	70	57	96	48
Right knee					
MT India Ink Staining (%)	1.54	9.57	2.37	8.10	3.46
MT microCT BV/TV (%)	44.98	28.39	15.28	32.16	12.13
MT MRI BV/TV (%)	8.52	2.00	2.18	3.11	0.43
Left knee					
MT India Ink Staining (%)	7.60	3.51	2.28	8.26	11.01
MT microCT BV/TV (%)	33.74	31.79	15.55	38.11	14.26
MT MRI BV/TV (%)	12.66	2.24	2.34	1.68	1.77

Notes: MT = medial tibia, BV/TV = bone volume fraction, microCT = micro-computed tomography, MRI = magnetic resonance imaging. Greater India ink staining is associated with greater cartilage damage.

Methods: Fresh cadaveric bilateral whole knee specimens were procured by the National Disease Research Interchange. Donors were selected if their age was 51 to 80 years and both knees had no pathology, with the exception of OA. Each specimen included tissue 8cm proximal and distal to the articular surface of the tibiofemoral joint. The knees were collected within 10 hours of death, packed in wet ice or ice packs, and sealed for shipping. Within 36 hours of death, the knees were imaged with a coronal-oblique 3-dimensional fast imaging with steady state precession (3D FISP) sequence using a Siemens Trio 3-Tesla MR system. Each knee was then repackaged with ice packs and sent to another facility for microCT analysis. The knees were placed in a 10% formalin solution within 58 hours of death. After preservation in formalin, a subchondral region from the tibial plateau was collected using a bone saw and imaged with a Skyscan 1172 (11 MPix camera) microCT scanner at 9μm resolution. A single reader analyzed the coronal 3D FISP images with a previously validated analysis tool. To analyze the MR-based trabecular morphometry, a rectangular region of interest (ROI) was positioned on the 20 consecutive central MR images in the proximal medial tibial subchondral bone. The ROI had a constant height of 3.75mm and width of 15.00mm. A different reader used Skyscan CT Analyzer software to measure structural indices from the microCT images in a similar volume of interest (17 x 13.73 x 3.94mm). The primary outcome measure was trabecular bone volume per total volume (BV/TV) in the proximal medial tibia. Spearman correlations were used to evaluate the association between MR-based and microCT-based BV/TV. Each knee was considered an independent measurement.
Results: The table provides demographic and quantitative data from each cadaver. In the proximal peri-articular medial tibia, MR-based apparent BV/TV was systematically lower than BV/TV values from microCT images. The MR-based apparent BV/TV had a moderate-good correlation with microCT-based BV/TV ($r = 0.58$, confidence interval = -0.08 to 0.89). When microCT data was restricted to trabeculae with larger trabecular thickness the correlation with MR-based apparent BV/TV was decreased ($r = 0.28$).
Conclusions: MR-based apparent BV/TV in the proximal peri-articular medial tibia has good validity and may represent an alternative for microCT-based BV/TV. The MR-based apparent BV/TV is systematically lower than microCT-based BV/TV potentially because we used conservative signal-intensity thresholds to define trabeculae, MR does not measure bone directly, post-mortem changes in the marrow signal may influence MR signal characteristics, and MR spatial resolution (1000 x 230 x 230μm) is lower than microCT (9 x 9 x 9μm) therefore partial volume averaging may reduce how discernible trabeculae appear.

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RESPONSIVENESS OF COMPARTMENT-SPECIFIC QUANTITATIVE CARTILAGE MRI MEASURES IN KNEE OA PATIENTS

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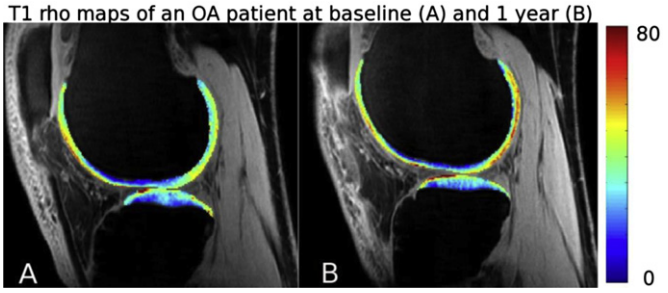
Purpose: Magnetic resonance imaging (MRI) has become a major and powerful tool to assess joint structural changes in osteoarthritis (OA). Accurate and non-invasive MR imaging techniques to detect changes in cartilage structure and composition are critical to track the progression of OA and to monitor treatment effects. Hence, it is essential to evaluate the responsiveness of these imaging techniques. The main aim of this study is to evaluate the responsiveness of compartment specific morphological and compositional cartilage MRI measures in knee OA patients.
Methods: MR data for 36 subjects (20 women; 16 men; age 53±10 years; BMI 26.7±4.5) were acquired at baseline and 1 year on a 3T Signa HDx MR (GE Healthcare, Piscataway, NJ) scanner with an 8-channel phased array knee coil. Sagittal cartilage T1ρ and T2 maps were generated using 3D MAPSS mapping technique (TR/TE=9.3/3.7 ms; FOV=14cm, matrix=256 × 128, slice thickness=4 mm, BW=31.25 kHz, views per segment=64, recovery time =1.5 s, for T1ρ: Time of Spin-Lock=0, 10, 40, 80 ms, spin-lock frequency=500 Hz; for T2: prep TE=4.1, 14.5, 25, 45.9 ms). A fat-saturated T1-weighted 3D SPGR sequence (TR/TE=15/6.7 ms, flip angle=12, FOV=14cm, matrix=512 × 512, slice thickness=1 mm, bandwidth=31.25 kHz, NEX=1) was used for cartilage segmentation and calculation of cartilage thickness and volume. Six cartilage knee compartments (lateral femoral condyle (LFC), medial femoral condyle (MFC), lateral tibia (LT), medial tibia (MT), and patella (PAT)) were segmented in a MATLAB (MathWorks, Natick MA) based in-house software package. Compartments were partitioned into a bone and articular layer, using a Euclidean distance algorithm with the same in-house software. Standardized response mean (SRM) was calculated for each MRI measure between baseline and 1 year as the mean of change divided by the standard deviation of change.
Results: The patients were grouped according to the severity of OA (KL grade 1-3). All compartment relaxation times were responsive for changes in the cartilage. The best cartilage thickness SRM was for patella (-0.75) from KL grade 2. The best T1ρ SRM values for full thickness cartilage, bone layer and articular layer were observed for LFC (0.53, KL grade 2; -0.54 for KL grade 3 and 0.54 for KL grade 2 respectively). Patella from KL grade 1 showed responsive SRM value for T1ρ bone layer (0.58). The best T2 SRM was for MT (0.99 from KL grade1) for T2 bone layer SRM it was LT (-0.66 from KL grade 3) and for T2 articular layer SRM it was LFC (-0.49 from KL grade 1).
Conclusion: These results suggest that the cartilage MRI measures are responsive to cartilage changes in knee OA patients. We have also showed that the relaxation rates of individual compartments are sensitive to cartilage changes. Moreover, changes in SRM values vary depending on cartilage compartment, and behave differently based on disease severity. These results suggest that these metrics could be used as responsive outcome measures in prospective clinical trials.



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CARTILAGE T1ρ AND T2 ARE ASSOCIATED WITH PATIENT-REPORTED OUTCOMES AFTER ACUTE ACL INJURIES

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Purpose: Anterior cruciate ligament (ACL) injury has been suggested as a high risk factor for post-traumatic osteoarthritis (OA) development. Previous studies reported significantly elevated MRI T1ρ and T2 in cartilage after acute ACL injuries. The goal of this study was to evaluate the relationship between cartilage MRI T1ρ and T2 quantifications and patient-reported outcomes after acute ACL injuries.

Table 1
Characteristics and KOOS scores of female and male patients with acute ACL injuries.

	Age (Years)	BMI (kg/m^2)	Pain	Symptoms	ADL	Sport/Rec	QoL
Female	29.7 ± 8.0	23.2 ± 1.9	73.8 ± 12.0	58.0 ± 19.4	78.1 ± 10.7	45.6 ± 24.9	34.0 ± 20.5
Male	29.6 ± 1.0	25.4 ± 3.5	73.2 ± 20.8	67.9 ± 20.7	85.3 ± 19.3	56.1 ± 25.4	38.8 ± 19.5
P values	1.0	0.1	0.9	0.3	0.3	0.3	0.6

Table 2
Correlation coefficients, R (P values), between KOOS and cartilage T1ρ and T2.

KOOS	T1ρ			T2			
	LFC	LT	PAT	LFC	LT	PAT	MFC
Pain	NS	NS	-0.43 (0.07)	NS	NS	-0.46 (0.05)	NS
ADL	-0.44 (0.07)	-0.61 (0.004)	-0.51 (0.03)	-0.62 (0.004)	NS	-0.72 (0.001)	-0.54 (0.02)
QoL	NS	NS	-0.49 (0.04)	NS	NS	-0.48 (0.004)	-0.58 (0.007)

Methods: Twenty-three patients with acute ACL injuries (9 females, age = 29.6 ± 7.0 years) were scanned after injury and before ACL reconstruction (time from injury to MR scan: 58 ± 40 days) using a 3 Tesla GE MR scanner and an 8-channel phased array knee coil. All patients filled in the Knee injury and Osteoarthritis Outcome Score (KOOS) during the MR visit. KOOS is a validated patient self-administered questionnaire that consists of 5 subscales: pain, other symptoms, activities in daily living (ADLs), function in sport and recreation (Sport/Rec), and knee-related quality of life (QoL) (100 indicating no symptoms and 0 indicating extreme symptoms). The imaging protocol included sagittal T2-weighted 3D fast spin-echo (FSE) images (CUBE) and sagittal 3D T1ρ and T2 quantification sequences (T1ρ: time of spin-lock = 0/10/40/80 ms, spin lock frequency = 500Hz; T2: preparation TE = 0/13.7/27.3/54.7ms). Cartilage was segmented semi-automatically in CUBE images into six compartments: lateral/medial femoral condyle (LFC/MFC), lateral/medial tibia (LT/MT), patella (PAT) and trochlea (TRO). The regions of interest were overlaid to reconstructed T1ρ and T2 maps after registration, and the mean T1ρ and T2 values were calculated in each compartments. The Spearman correlation coefficients between each subscales of KOOS, age, body mass index (BMI), time to injury and T1ρ and T2 values in each compartment were calculated.
Results: KOOS scores decreased significantly with increased age (R = -0.53, P=0.01 for SportsRec; R = -0.37∼-0.39, P = 0.06 ∼ 0.08 for the other 4 subscales), slightly decreased in female patients compared to male patients in all subscales except for pain (Table 1), slightly increased with increased time to injury in all subscales (R = 0.22 ∼ 0.34, P = 0.1 ∼ 0.3) except for Sprot/Rec (R = 0.1, P = 0.6) and showed no significant correlation with BMI (all R 0.5). Significant correlations were observed between MRI T1ρ and T2 (especially in LFC, LT and PAT) and KOOS (especially with the subscale of ADL) after adjusted for age, gender and time to injury, Table 2.
Discussion and Conclusions: In this study, older age was associated with worse patient-reported outcomes (lower KOOS) and there was a trend of worse outcomes in female patients compared to male patients after acute ACL injuries, which are consistent with previous reports by Ageberg et al and Dunn et al. Quantitative MRI, such as T1ρ and T2, are sensitive for detecting early degeneration in the cartilage matrix. In this study, significant correlations were observed between KOOS and cartilage T1ρ and T2 after adjusted for age, gender and time to injury, indicating an independent relationship between cartilage damage and patient outcomes after acute injuries. Interestingly, in this study, the correlations between KOOS and T1ρ and T2 measures are located not only in the lateral side (LFC and LT, the primary injury side after ACL tear), but also in the patella and MFC, suggesting a global disturbance of cartilage homeostasis within the whole joint after the injury. We are currently recruiting more patients to confirm these findings and will follow up the patients after ACL reconstruction to explore the longitudinal relationship between patient outcomes and cartilage T1ρ and T2.

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MEDIAL MENISCAL PATHOLOGY IS ASSOCIATED WITH PERIARTICULAR BONE MEASURES: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: Damaged menisci have impaired ability to distribute load within the knee. Bone responds to load that is applied to a joint. In prior studies medial tibiofemoral knee osteoarthritis (OA) has been associated with peri-articular bone measures that could be consistent with remodeling or microtrauma. Therefore, we expect that medial meniscal damage would be associated with measures of adjacent peri-articular bone that are reflective of abnormal loading and OA.
Methods: We studied participants in the Osteoarthritis Initiative (OAI) with at least one knee with symptomatic knee OA, who had the OAI core set of magnetic resonance (MR) images at the 24-month visit, and who consented to dual-energy x-ray absorptiometry (DXA) and additional MR imaging at the 30-/36-month OAI visits. The right knee was selected as the index knee for these participants unless there was a contraindication for MR imaging; therefore, the index knee did not have OA as a pre-requisite. A single musculoskeletal radiologist scored the 24-month OAI core images for meniscal pathology by region (e.g., anterior, body, and posterior horn) within the medial menisci using a modified International Society of Arthroscopy, Knee Surgery, and Orthopaedic Sports Medicine (ISAKOS) meniscal tear classification system. To simplify the classification system we focused on two definitions: 1) presence of any medial meniscal pathology (absent, present) and 2) number of regions in the medial meniscus with meniscal maceration (none, one, two or more). To quantify trabecular morphometry, one reader measured 3T coronal-oblique 3D fast imaging with steady state precession (FISP) images from the 30- or 36- month visit with a previously validated program. MR-based trabecular morphometry measures [apparent bone volume fraction (a.BV/TV), trabecular number (a.Tb.N), trabecular thickness (a.Tb.Th), and trabecular spacing (a.Tb.Sp)] were evaluated in the proximal medial tibial subchondral bone. Using investigational software, knee DXAs were obtained at the 30- or 36-month visit providing measures of medial:lateral periarticular bone mineral density ratios (M:L paBMD). Standard hip DXAs measured femoral neck (systemic) bone mineral density (BMD). T-tests compared baseline characteristics, systemic BMD, and peri-articular bone measures in those with and without medial meniscal pathology. Analyses of variance (ANOVA) were used to compare knees by number of medial meniscal maceration regions. Because few knees had

Table 1
Peri-articular bone measures are different between knee with and without medial meniscal pathology

	Medial Meniscal Pathology		p-value
	Absent (n = 114)	Present (n = 350)	
Age (years)	60.43(± 8.50)	65.17(± 9.07)	<0.0001
Body Mass Index (BMI) (kg/m^2)	30.01(± 15.21)	29.32 (± 4.41)	0.20
Systemic BMD	0.96(± 0.15)	0.96(± 0.15)	0.89
M:L paBMD	1.05(0.13)	1.14(0.15)	<0.0001
a.BV/TV	0.09(± 0.06)	0 11(± 0.07)	0 02
a.Tb.N (mnr^{-1})	0.73(± 0.33)	0.81(± 0.37)	0 05
a.Tb.Th (mm)	0.12 (± 0.02)	0 13 (± 0.02)	0.02
a.Tb.Sp (mm)	1.79(± 1.55)	1.63 (± 1.25)	0.29

Note: BV/TV = bone volume divided by total volume (bone volume fraction); a.Tb.N = apparent Trabecular Number; a.Tb.Th = apparent Trabecular Thickness; a.Tb.Sp = apparent Trabecular Spacing.